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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,210	03/27/2001	Shlomo Margel	LUZZ-051CIP	7952
530	7590	12/15/2004	EXAMINER	
LERNER, DAVID, LITTENBERG, KRUMHOLZ & MENTLIK 600 SOUTH AVENUE WEST WESTFIELD, NJ 07090			SHARAREH, SHAHNAM J	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/701,210	MARGEL ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2004.
- 2a) ☐ This action is **FINAL**.      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 7-48 is/are pending in the application.
- 4a) Of the above claim(s) 33-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-32, 47 and 48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 6, 2004 has been entered.

Claims 1-5, 7-48 are pending. Applicant's arguments with respect to the pending claims have been considered but are moot in view of the new ground(s) of rejection.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7-32, 47-48 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are directed to making magnetic iron oxide and ferrite nanoparticles. However, no iron oxide or ferrite is used during any steps of the claimed invention. The omitted steps is: the incorporation or addition of iron oxide and ferrite to the mixture during steps b-f.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 47-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Elaissari et al US Patent 6,133,047.

Elaissari discloses methods of preparing monodispersed particles in ranges of 01  $\mu\text{m}$ . (col 10, lines 55-57). Therefore, Elaissari meets the limitations of the instant nanoparticles. Elaissari's methods comprise preparing an aqueous solution of a first and a second polymer, adding an aqueous anionic ferrofluid comprising iron oxides solution at pH 6-8, causing the polymer and the iron oxide to interact electorstatically. (See abstract, col 8-9, specifically examples 2-3). The ferrofluid of Elaissari meets the limitation of the instant metal ions. The polymeric solution of Elaissari also meets the limitation of the instant polymeric metal chelating agent, because it comprise functional groups such as hydroxyl, carboxylates, immine or amino. (see col 3, lines 5-50). Elaissari progressively adds the polymeric solutions and the ferrofluid. (col 9, lines 5-7).

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Such step is viewed to meet the instant limitation of successively adding the solutions together. Elaissari meets all the limitations of the instant claims.

Claims 1-5, 7-32, 47-48 rejected under 35 U.S.C. 102(b) as anticipated Margel US Patent 4,783,336.

Margel discloses methods of preparing an coated acrolein type in nanometer sizes comprising mixing an aqueous solution of acrolein with an aqueous dispersion of  $\text{Fe}_3\text{O}_4$  in presence of an oxidizing agent at pH values above 7 to form magnetic particles of uniform size, wherein said particles are cross linked to various bioactive agents such as immunoglobulin or fluorescent dyes for various utilities such as cell labeling, cell separation, diagnostic purposes, etc.. (see col 1, lines 10-62, examples 3, 20, 27; and claims 1, 4-13).

The formation addition of ferrofluidic solution to polymeric solution of Margel occurs over a 12 hours period. (see col 6, lines 40-55). Examiner has taken the position that Margel's process of adding the metallic solution to the polymeric solution meets the limitations of the instant step (g) because it is done during a 12 hour period and the instant step does not exclude the process described by Margel. Therefore, such step is viewed to meet the instantly claimed step of successively repeating the step (a) to (f) of the claim 1.

Margel's method employs polymerizing acrolein to form anionic polyacrolein microspheres at pH of about 13. (col 2, line 47; col 3, line 32). Such polymers are within the scope of the instant claims because they are anionic and contain hydroxyl, carboxyl, ether groups. (see col 2, lines 40-50; col 1, lines 45-62). Margel states that anionic

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polymers such as PolyvinylPyridine may be coated in the same manner as the polyacrolein beads (col 3, lines 51-56).

Note that Margel uses a nitrate salt oxidizing agent such as persulfate-silver nitrate which meets the limitations of claims 12-15. (col 2, lines 51-65). Margel uses a basic surfactant or solution to maintain a high pH during his microsphere formation which meets the limitations of claims 17-18 (see col 3, lines 25-35; col 4, lines 40-51).

Margel employs diagnostic agents such as rhodamine isothiocyanate to prepare fluorescent microspheres (col 4, line 65-col 5, line2). Margel finally labels other biological molecules with the polyacrolein microspheres meeting claims 24-32 (col 7, line 65-col 8, line22). Accordingly Margel is viewed to meet all limitations of the instant claims.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-32, 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elaissari et al US Patent 6,133,047 in view of Hirai US Patent 5,213,895

The teachings of Elaissari are described above. Elaissari further teaches attaching a biological molecule such as an antibody etc.. to the particles directly or via a ligand (col12, lines 34-55). Elaissari fails to use polymeric solutions such as polyvinylpyrrolidone or gelatin or a nitric acid oxidizer for his process.

Hirai teaches methods of preparing nanoparticles comprising preparing a polymeric solution such as polyvinylpyrrolidone or gelatin and adding an aqueous metallic solution to the polymeric moiety (see col 9, lines 25-60; col 12, lines 14-65; col 13, line 62-col 14, lines 67). The process of Hirai leads to formation of magnetite particles which meets the limitations of the instant magnetic iron oxide. (col 14, lines 45-67). The polymeric solution of Hirai contains a concentration (col 8, lines 14-18). Hirai describes the use of nitrate ion as oxidizer (col 19, lines 30-36).

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Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to perform Elaissari's methodology with other suitable polymeric solutions such as those described by Hirai, because as taught by Hirai, such polymeric moieties are expected to provide similar results as those used by Elaissari. Further using an oxidizing agent during the process of oxidation is a matter of design choice and merely selecting a nitrate for such purpose would have been obvious absence of showing an unexpected result.

### ***Conclusion***

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 SHENGJUN WANG  
PRIMARY EXAMINER